AMENDMENTS

IN THE SPECIFICATION

Please replace the Sequence Listing with the enclosed substitute Sequence Listing, provided as separately numbered pages 1-13

Please replace the paragraph bridging pages 10-11 with the following:

Alternative 5' variants of the human VDR gene were identified by 5'RACE using commercially prepared anchor-ligated cDNA (Clontech) following the instructions of the manufacturer. Two rounds of PCR using nested reverse primers in exons 3 and 2 (P 1: 5'ccgcttcatgcttcgcctgaagaagcc-3' **(SEQ ID NO: 23)**, P2: 5'-tgcagaattcacaggtcatagcattgaag-3' **(SEQ ID NO: 24)**) were carried out on a Corbett FTS-4000 Capillary Thermal Sequencer (Corbett Research, NSW, Australia). After 26 cycles of PCR, 2% of the primary reaction was reamplified for 31 cycles. The PCR products were cloned into PUC18 and sequenced by the dideoxy chain termination method.

Please replace the paragraph bridging pages 11-12 with the following:

Total RNA extracted from approximately 1.5 x 10^3 cells, from leukocytes prepared from 40 ml blood, or from human tissue using acid-phenol extraction was purified by using a guanidium isothiocyanate-cesium chloride step gradient. First-strand cDNA was synthesized from 5 Tg of total RNA primed with random hexamers (Promega) using Superscript II reverse transcriptase (Life Technologies). One-tenth of the cDNA (2Tl) was used for subsequent PCR, with 36 cycles of amplification, using exon-specific forward primers (exon 1a: corresponding to nucleotides 1–21 of hVDR cDNA (1);

exon 1d: 5'~~(SEQ ID NO: 13)~~ -GGCTGTCGATGGTGCTCAGAAC-3' **(SEQ ID NO: 25)**;

exon 1f: 5'~~(SEQ ID NO: 14)~~ -AAGTTCCTCCGAGGAGCCTGCC-3' **(SEQ ID NO: 26)**);

and a common reverse primer in exon 3 [corresponding to nucleotides 301–280 of hVDR cDNA (1)]. All RT-PCRs were repeated multiple times by using RNA/cDNA prepared at different times from multiple sources. Each PCR included an appropriate cDNA-negative control, and additional controls included RT-negative controls prepared alongside cDNA and RNA/cDNA prepared from VDR-negative cell lines. PCR products were separated on 2% agarose and visualized with ethidium bromide staining.

Please replace the paragraph bridging pages 16-17 with the following:

Heterogeneity in the 5' region is a common feature of other nuclear receptor genes. Tissue-specific alternative-promoter usage generates multiple transcripts of the human estrogen receptor a (ERa), the human and rat mineralocorticoid receptors, and the mouse glucocorticoid receptor (GR), which differ in their 5' UTRs but code for identical proteins. However, other members of the nuclear receptor superfamily have multiple, functionally distinct isoforms arising from differential promoter usage and/or alternative splicing. The generation of N-terminal variant protein isoforms has been described for the progesterone receptor (PR), peroxisome proliferator-activated receptor ($PPAR_o$), and the retinoid and thyroid receptors. Some receptor isoforms exhibit differential promoter-specific transactivation activity. The N-terminal A/B regions of many nuclear receptor proteins possess a ligand-independent transactivation function (AF1). An AF1 domain has been demonstrated for the thyroid receptor b1 (TRb1), ER, GR, PR, PPARg, and the retinoid receptors. The activity of the AF1 domain has been shown to vary in both a tissue- and promoter-specific manner. The N-terminal A/B region of nuclear receptors is the least-conserved domain across the family and between receptor subtypes, varying considerably both in length and sequence. The VDR, however, is unusual as its N-terminal A/B region is much shorter than that of other nuclear receptors, with only 23 aa N-terminal to the DNA-binding domain, and deletion of these residues seems to have no effect on VDR function. This region in other receptors is associated with optimal ligand-dependent transactivation and can interact directly with components of the basal transcription complex. Two stretches of basic amino acid residues, RNKKR **(SEQ ID NO: 27)** and RPHRR **(SEQ ID NO: 28)**, in the predicted amino acid sequences of the variant hVDR N termini (Fig. 1*C*) resemble nuclear localization signals. An N-terminal variant VDR protein therefore might exhibit different transactivation potential, possibly mediated by different protein interactions, or may specify a different subcellular localization. The tissue-specific expression of exon 1f-containing transcripts is mediated by a distal promoter more than 9 kb upstream of exons 1a and 1d. Exon 1f transcripts were detected only in kidney tissue, parathyroid adenoma tissue, and an intestinal cell line, LIM 1863. It is interesting that these tissues represent major target tissues for the calcitropic effects of vitamin D. The absence of 1f-containing transcripts in two other kidney cell lines, HK-2 (proximal tubule) and HEK-293 (embryonal kidney), as well as one other embryonal intestinal cell line, Intestine-407, suggests that the expression of 1f transcripts is cell type-specific. The cell line-specific activity of exon 1f flanking sequences in promoter reporter assays may reflect a requirement for tissue- or cell-specific protein factors to mediate expression from this promoter.